

PANDEL - hydrocortisone probutate cream

PharmaDerm, A division of Nycomed US Inc.

Rx only

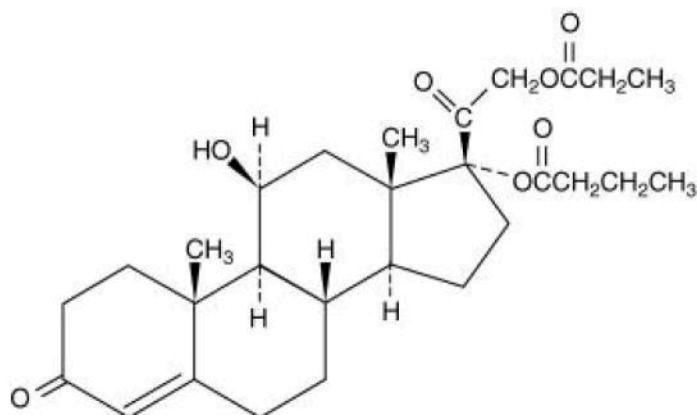
For Dermatologic Use Only

Not for Ophthalmic Use

DESCRIPTION

Pandel[®] Cream contains hydrocortisone probutate, a synthetic adrenocorticosteroid, for dermatologic use. The topical corticosteroids constitute a class of primarily synthetic steroids used as anti-inflammatory and anti-pruritic agents.

Hydrocortisone probutate is a tasteless and odorless white crystalline powder practically insoluble in hexane or water, slightly soluble in ether, and very soluble in dichloromethane, methanol and acetone. Chemically, it is 11 β ,17,21-trihydroxypregn-4-ene-3,20-dione 17-butyrate 21-propionate. The structural formula is:



Molecular Formula: C₂₈H₄₀O₇

Molecular Weight: 488.62

Each gram of Pandel (hydrocortisone probutate cream) Cream, 0.1% contains: 1 mg of hydrocortisone probutate in a cream base of propylene glycol, white petrolatum, light mineral oil, stearyl alcohol, polysorbate 60, sorbitan monostearate, glyceryl monostearate, PEG-20 stearate, glyceryl stearate SE, methylparaben, butylparaben, citric acid, sodium citrate anhydrous, and purified water.

CLINICAL PHARMACOLOGY

Topical corticosteroids share anti-inflammatory, anti-pruritic and vasoconstrictive actions. The mechanism of anti-inflammatory activity of the topical corticosteroids is unclear. However, corticosteroids are thought to act by the induction of phospholipase A₂ inhibitory proteins, collectively called lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A₂.

Pharmacokinetics: The extent of percutaneous absorption of topical corticosteroids is determined by many factors, including the vehicle and the integrity of the epidermal barrier. Use of occlusive dressings with hydrocortisone for up to 24 hours has not been shown to increase penetration; however, occlusion of hydrocortisone for 96 hours does markedly enhance penetration. Topical corticosteroids can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin increase percutaneous absorption.

Studies performed with Pandel (hydrocortisone probutate cream) Cream, 0.1% indicate that it is in the medium range of potency compared with other topical corticosteroids.

INDICATIONS AND USAGE

Pandel (hydrocortisone probutate cream) Cream, 0.1% is a medium potency corticosteroid indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses in patients 18 years of age or older.

CONTRAINDICATIONS

Pandel (hydrocortisone probutate cream) Cream, 0.1% is contraindicated in those patients who are hypersensitive to hydrocortisone probutate or to any of the components of the preparation.

PRECAUTIONS

General: Systemic absorption of topical corticosteroids can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment. Manifestations of Cushing's syndrome, hyperglycemia, and glucosuria can also be produced in some patients by systemic absorption of topical corticosteroids while on treatment.

Patients applying a topical steroid to a large surface area or to areas under occlusion should be evaluated periodically for evidence of HPA-axis suppression. This may be done by using the ACTH stimulation, A.M. plasma cortisol or urinary free cortisol tests. If HPA axis suppression is noted, an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute a less potent steroid. Recovery of HPA axis function is generally prompt and complete upon discontinuation of the drug. Infrequently, signs and symptoms of steroid withdrawal may occur, requiring supplemental systemic corticosteroids. For information on systemic supplementation, see prescribing information for those products.

Pediatric patients may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratios. (See **PRECAUTIONS–Pediatric Use**).

If irritation develops, Pandel (hydrocortisone probutate cream) Cream, 0.1% should be discontinued and appropriate therapy instituted. Allergic contact dermatitis with corticosteroids is usually diagnosed by observing a failure to heal rather than noting a clinical exacerbation, as observed with most topical products not containing corticosteroids.

If concomitant skin infections are present or develop, an appropriate antifungal or antibacterial agent should be used. If a favorable response does not occur promptly, use of Pandel (hydrocortisone probutate cream) Cream, 0.1% should be discontinued until the infection has been adequately controlled.

Information for Patients: Patients using Pandel (hydrocortisone probutate cream) Cream, 0.1% should receive the following information and instructions:

1. This medication is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes.
2. This medication should not be used for any disorder other than that for which it was prescribed.
3. The treated skin area should not be bandaged or otherwise covered or wrapped so as to be occlusive, unless directed by the physician.
4. Patients should report to their physician any signs of local adverse reactions.
5. Parents of pediatric patients should be advised not to use Pandel (hydrocortisone probutate cream) Cream, 0.1% in the treatment of diaper dermatitis. Pandel (hydrocortisone probutate cream) Cream, 0.1% should not be applied in the diaper area as diapers or plastic pants may constitute occlusive dressings (See **DOSAGE AND ADMINISTRATION**).
6. This medication should not be used on the face, underarms, or groin areas unless directed by the physician.
7. As with other corticosteroids, therapy should be discontinued when control is achieved. If no improvement is seen within two weeks, contact the physician.

Laboratory Tests: The following tests may be helpful in evaluating if HPA axis suppression does occur:

ACTH stimulation test

A.M. plasma cortisol test

Urinary free cortisol test

Carcinogenesis, Mutagenesis and Impairment of Fertility: Long-term animal studies have not been performed to evaluate the carcinogenic potential or the effect on fertility of topical corticosteroids.

In two mutagenicity experiments using hydrocortisone probutate, negative responses were observed in the occurrence of micronuclei in the bone marrow of mice and in the Ames reverse mutation test bacterial assay - with and without metabolic activation.

Pregnancy: Teratogenic Effects–Pregnancy Category C. Corticosteroids have been shown to be teratogenic in laboratory animals when administered systemically at relatively low dosage levels. Some corticosteroids have been shown to be teratogenic after dermal application to laboratory animals.

Hydrocortisone probutate has not been tested for teratogenicity when applied topically; however, it is absorbed percutaneously, and studies in Wistar rats using the subcutaneous route resulted in teratogenicity at dose levels equal to or greater than 1 mg/kg. This dose is approximately 12 times the human average topical dose of Pandel Cream, 0.1% assuming 3% absorption and an application of 30 g/day on a 70 kg individual. Abnormalities seen included delayed ossification of the caudal vertebrae and other skeletal variations, cleft palate, umbilical hernia, edema, and exencephalia.

In rabbits, hydrocortisone probutate given by the subcutaneous route was teratogenic at doses equal to or greater than 0.1 mg/kg. This dose is approximately 2 times the human average topical dose of Pandel Cream, 0.1% assuming 3% absorption and an application of 30 g/day on a 70 kg individual. Abnormalities seen included delayed ossification of the caudal vertebrae and other skeletal abnormalities, cleft palate and increased fetal mortality.

The differences between the doses used in animal studies and the proposed human dose may not fully predict the human outcome.

The animals received a bolus subcutaneous dose, whereas humans receive a dermal application, where absorption is lower and highly dependent on various factors (e.g., vehicle, integrity of epidermal barrier, occlusion).

There are no adequate and well-controlled studies of the teratogenic potential of hydrocortisone probutate in pregnant women.

Although human epidemiological studies do not indicate an increased incidence of teratogenicity with the use of topical corticosteroids, Pandel Cream should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Because many drugs are excreted in human milk, caution should be exercised when Pandel (hydrocortisone probutate cream) Cream, 0.1% is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in pediatric patients have not been established. Because of a higher ratio of skin surface area to body mass, pediatric patients are at a greater risk than adults of HPA axis suppression and Cushing's syndrome when they are treated with topical corticosteroids. They are therefore also at a greater risk of adrenal insufficiency during and/or after withdrawal of treatment. Adverse effects including striae have been reported with inappropriate use of topical corticosteroids in infants and children. Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, linear growth retardation, delayed weight gain, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include low plasma cortisol levels and an absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

ADVERSE REACTIONS

The most frequent adverse reactions reported for Pandel (hydrocortisone probutate cream) Cream, 0.1% have included burning in 4, stinging in 2, and moderate paresthesia in 1 out of 226 patients.

The following local adverse reactions are reported with topical corticosteroids, and they may occur more frequently with the use of occlusive dressings. These reactions are listed in an approximate decreasing order of occurrence: burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infections, skin atrophy, striae, miliaria.

OVERDOSAGE

Topically applied corticosteroids can be absorbed in sufficient amounts to produce systemic effects. (See **PRECAUTIONS**).

DOSAGE AND ADMINISTRATION

Apply a thin film of Pandel (hydrocortisone probutate cream) Cream, 0.1% to the affected area once or twice a day depending on the severity of the condition. Massage gently until the medication disappears.

Occlusive dressings may be used for the management of refractory lesions of psoriasis and other deep-seated dermatoses, such as localized neurodermatitis (lichen simplex chronicus).

As with other corticosteroids, therapy should be discontinued when control is achieved. If no improvement is seen within 2 weeks, reassessment of the diagnosis may be necessary.

Pandel (hydrocortisone probutate cream) Cream, 0.1% should not be used with occlusive dressings unless directed by the physician.

Pandel (hydrocortisone probutate cream) Cream, 0.1% should not be applied in the diaper area, as diapers or plastic pants may constitute occlusive dressings.

HOW SUPPLIED

Pandel (hydrocortisone probutate cream) Cream, 0.1%, a white to off-white opaque cream is supplied as follows:

15 g tubes NDC 0462-0153-15

45 g tubes NDC 0462-0153-46

80 g tubes NDC 0462-0153-80

Store at controlled room temperature 15°-30°C (59°-86°F).

PharmaDerm®

A division of Nycomed US Inc.

Melville, NY 11747 USA

www.pharmaderm.com

I8153A/IF8153A

R12/08

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PACKAGE LABEL – PRINCIPAL DISPLAY PANEL – 15g LABEL

NDC 0462-0153-15

PharmaDerm

Pandel

(hydrocortisone probutate) Cream, 0.1%

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15g



PACKAGE LABEL – PRINCIPAL DISPLAY PANEL – 15g CARTON

NDC 0462-0153-15

PharmaDerm

Pandel

(hydrocortisone probutate) Cream, 0.1%

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Rx only

15g



PACKAGE LABEL – PRINCIPAL DISPLAY PANEL – 45g LABEL

NDC 0462-0153-46

PharmaDerm

Pandel

(hydrocortisone probutate) Cream, 0.1%

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Rx only

45g



PACKAGE LABEL – PRINCIPAL DISPLAY PANEL – 45g CARTON

NDC 0462-0153-46

PharmaDerm

Pandel

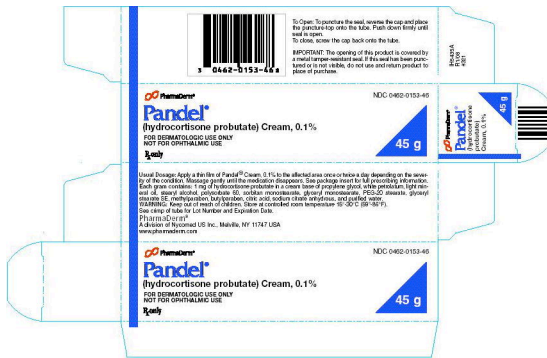
(hydrocortisone probutate) Cream, 0.1%

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45g



PACKAGE LABEL – PRINCIPAL DISPLAY PANEL – 80g LABEL

PharmaDerm

Pandel

(hydrocortisone probutate) Cream, 0.1%

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Not for Ophthalmic Use

Rx only

80g



PACKAGE LABEL – PRINCIPAL DISPLAY PANEL – 80g CARTON

PharmaDerm

Pandel

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